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SENNIGER POWERS LLP (ILPS)
100 NORTH BROADWAY
17TH FLOOR
ST. LOUIS, MO 63102

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**BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

Application Number: 10/814,749
Filing Date: March 30, 2004
Appellant(s): CHARMOT ET AL.

Janet S. Hendrickson, Ph.D.
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 3/18/10 appealing from the Office action mailed 9/18/09.

**(1) Real Party in Interest**

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The following is a list of claims that are rejected and pending in the application:

Claims 3, 4, 15, 21, 29, 30, 34, 40, 51-64 and 66-76 are pending. Claims 1-2, 5-14, 16-20, 22-28, 31-33, 35-39, 41-50 and 65 are canceled.

**(4) Status of Amendments After Final**

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

**(5) Summary of Claimed Subject Matter**

The examiner has no comment on the summary of claimed subject matter contained in the brief.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except

for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

**(7) Claims Appendix**

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

**(8) Evidence Relied Upon**

| | | |
|---|---|---|
| EP 0 730 494 | NOTENBOMBER | 02-1998 |
| 6,558,665 | COHEN | 05-2003 |
| 4,380,590 | CHONG et al | 04-1983 |
| 5,824,339 | SHIMZU | 10-1998 |
| 3,499,960 | MACEK et al | 03-1970 |

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 4, 15, 21, 29, 30, 34, 51-59, 62-64, 66-73, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Notenbomer (EP 0 730 494 hereafter '494) in view of Cohen et al (USPN 6,558,665 hereafter '665). The claims are drawn to an oral formulation comprising core-shell particles wherein the core comprises a cation-exchange resin and the coating is hydrophobic.

The '494 patent discloses a particle formulation comprising a core and a coating where the core comprises a cation exchange resin and the coating does not disintegrate during passage through the intestinal tract of humans and where the membrane is more permeable to monovalent cations rather than bi-or higher cations (page 1, lin. 49-55). The particles can be mixed with sodium chloride as an excipient and administered orally as a foodstuff (page 2, lin. 54-60). The particles are safe means of absorbing cations from the digestive tract, encapsulating the ions and removing them as waste from the body (page 2, lines 8-12). The cation exchange materials come from a wide range of sources and can include sulphonated crosslinked polystyrenes, polycarboxylates, polymaleinates, polyacrylates and polyphosphates (page 2, lin. 20-34). The cation exchange resin of the reference can be used to remove potassium ions from a variety of sources (page 3, lin. 10-12). The coatings include polyethyleneimine and known surfactants (page 2, lin. 42-45; example 2). The particles can be further coated with cellulose acetate a well known enteric polymer (example 1). The reference is silent to the specific monomers of the instant claims. The particles are microcapsules that range in size from 0.01-10 mm in size, with

specific ranges of approximately 290 microns (page 2, lin. 41-42; Example 1). The particles can be formulated in various pharmaceutical forms including tablets, pills and capsules (page 3, lines 15-18). The thickness of the coating can be adjusted during the coating process, whether through fluidized bed coating or via interfacial polymerization. Coating thickness manipulation can be seen in the '665 patent.

The '665 patent discloses uniform coating surrounding particles (abstract). The coating is uniform from 10-20 microns thicken and can comprise a crosslinked polyethylene glycol (col. 7, lin. 15-20), along with other surfactants such as Poloxamer (col. 7, lin. 40-45). The coatings can be applied using interfacial polymerization (col. 7, lin. 58-60). Polystyrene particles measuring from 200-300 microns are coated with crosslinked polyethylene glycol at a thickness of 20 microns (example). That is a 0.1:1 ratio of components in order to achieve such as thickness and diameter. It would have been obvious to coat the particles of the '494 patent in a similar fashion of the '665 patent since they both use the same method to apply uniform coatings. Also it would have been obvious since the '665 patent used surfactants as coating agents as well.

Regarding the percentages of retained potassium ions, it is the position of the Examiner that such percentages would be obvious in view of the prior art. It is the position of the Examiner that these retention percentages are merely functional limitations that are inherent to the components of the instant claims. The '494 and '665 patents discloses coated particles comprising polymeric cores comprising the same components as those recited in the claims, specifically crosslinked styrene or sulphonic polymers, coated by crosslinked synthetic polymers with polymerized ethylenic monomers. The coatings are applied in the same thickness and for the same purpose of removing cations from the digestive system. Specific cations include

potassium. The combined disclosures meet the general conditions of the instant claims, and would inherently meet the functional limitations of the claims. Appellant is reminded that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredient(s). However, the preparation of various compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

Regarding the condition the human patient is suffering for, it is the position of the Examiner that such limitations are merely a future intended use for the dosage form, and do not obviate over the prior art. As discussed above the prior art combination discloses the same oral pharmaceutical formulation comprising the same components. The prior art discloses a structurally identical pharmaceutical formulation comprising the same components, as such the condition suffered by the patient is irrelevant to the formulation itself. Inclusion of the condition adds an implicit method of administration step to the product claim, meaning the limitations are product-by-process claims.

The Patent Office bears a lesser burden of proof in making out a case of prima facie obviousness for product-by-process claims because of their peculiar nature" than when a product is claimed in the conventional fashion. See *In re Fessmann*, 489 F.2d 742, 744, 180 USPQ 324,

326 (CCPA 1974). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to appellant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. See *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir.1983)

With these things in mind it would have obvious to coat the particles of the '494 patent in a uniform thickness as disclosed in the '665 patent. The patens disclose similar method of coating and comprise similar components, and as such it would have been obvious to coat the particles to a uniform thickness of 10-20 microns as disclosed in the '665 patent. One of ordinary skill in the art would have been motivated to combine the teachings disclosure and suggestions of the prior art as such with an expected result of a stable coated cation exchange resin useful in removing cations from the intestinal tract of a human.

Claims 3, 34, 40 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Notenbomer (EP 0 730 494 hereafter '494) and Cohen et al (USPN 6,558,665 hereafter '665) in view of Chong et al (USPN 4,380,590 hereafter '590). The claims are drawn to a method of treating hyperkalemia in a human patient in need of treatment with a pharmaceutical formulation comprising core-shell particles with a specific configuration.

As disclosed as the '494/'665 patent combination discloses a pharmaceutical product useful in removing specific ions from the intestinal tract of humans. The ions removed depend on the cation exchange resin in the core. The ions removed can be sodium, potassium or

ammonium. The reference is silent to specific disorders treated with this formulation; however it would be obvious to treat any conditions where ion reduction would be a treatment option.

The ‘590 patent discloses a cation exchange resin emulsion comprising a crosslinked copolymer component selected from the group consisting of styrene, vinyl, acrylic or methacrylic monomers (col. 5, lin. 15-52). Among the many uses for the cation exchange resin is a treatment for hyperkalemia (col. 9, lin. 35-55).

It would have been obvious to one of ordinary skill in the art to treat hyperkalemia with a cation exchange resin as disclosed in the prior art in order to sufficiently remove excess potassium ions from the body. Under the suggestion of the '590 patent to use acid cation ion exchange resins to treat hyperkalemia, the artisan of ordinary skill would have been motivated to apply the composition of the '494/'665 patent combination in order to remove excess potassium ions from the body effectively treating hyperkalemia in a human patient in need of treatment.

Claims 3, 53, 60, 61, 74 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined disclosures of Notenbomer (EP 0 730 494 hereafter '494) and Cohen et al (USPN 6,558,665 hereafter ‘665) in view of Shimzu et al (USPN 5,824,339 hereafter '339) and Macek et al (USPN 3,499,960 hereafter '960). The claims are drawn to a pharmaceutical formulation comprising core shell particles where the core is a cation exchange resin and the shell is a specific polymer.

As discussed above the combination of the ‘494/’665 patent discloses a pharmaceutical composition comprising core-shell particles with a desired shell and core. The combination is silent to the specific shell components of the instant claims. These shell components are well

known in the art and would have been obvious additions. The combination discloses the use of crosslinked ethylic monomers in the shell, and suggests any useful polymer that can be made permeable to the desired valent cation is useful. These coating components can be found in the '339 and '960 patents.

The '339 patent discloses a core-shell particle formulation comprising a shell component comprising crosslinked polyvinylpyrrolidone, and a core comprising carboxyl functional groups (col. 8, lin. Lin. 14-25; col. 6, lin. 36-51). The core-shell particles further contain excipients and stabilizers to make them more palatable for oral administration (examples). The '960 patent discloses a palatable ion exchange formulation comprising a coating of crosslinked acrylic polymers (abstract). The ion exchange resin includes crosslinked polystyrene resin and the coating is a crosslinked acrylic acid copolymer (col. 3, lin. 10-25).

It would have been obvious to include these shell components into the formulation of the '494/'665 combination in order to provide sufficient permeability of potassium ions into the cation exchange core. It would have been obvious to combine the teachings and suggestions in order to arrive at a palatable oral formulation useful in the treatment of a variety of ion related disorders.

**(10) Response to Argument**

Appellant's arguments filed 6/5/09 have been fully considered but they are not persuasive. Appellant argues that:

**The combination of the '494 and '665 patents does not obviate the claims since they are nonanalogous art and do not solve the same problem.**

Regarding this argument, it remains the position of the Examiner that the combination of the ‘494 and ‘665 patent continues to obviate the instant claims. In response to appellant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to appellant's argument that the ‘665 patent is nonanalogous art, it has been held that a prior art reference must either be in the field of appellant’s endeavor or, if not, then be reasonably pertinent to the particular problem with which the appellant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, the instant claims are drawn to a pharmaceutical composition comprising microparticles that are coated with a synthetic crosslinked polymer. The '665 patent explicitly discloses a microparticulate formulation comprising a core and coating where the coating is a crosslinked synthetic polymer. The coating is of the same thickness and composition of the instant claims. The coating is applied in order to provide a durable coating that does not disintegrate during use. The coated core-shell products of the ‘665 patent are used to remove harmful or unwanted compounds from the body (col. 9, lin. 40-46). This removal of compounds from the body by the use of coated core-shell particles places the '494 and the '665 patent in the same field of endeavor solving the same problem of removing compounds from the body using coated particles. As such the ‘665 patent constitutes analogous art. Regarding the combination, the ‘494 patent discloses an oral pharmaceutical dosage form comprising a core and shell, where the core is a cation-exchange resin. The

formulation is used to remove ions from a specific environment. The cores can be coated with any polymer. The microparticle is meant not to dissolve upon use. The '665 patent provides a stable and strong coating composition that prevents dissolution. Appellant continues to argue that the '494 and '665 patent are not within the same field of endeavor and solve different problems. However it appears that Appellant has defined the filed of endeavor too narrowly. The field of endeavor is simply the removal of compounds from the body using coated particles, which is a very similar pharmaceutical use. The '494 patent removes ions from the body using cation exchange resin cores that are coated. The '665 patent removes harmful compounds and metabolites using similarly coated core-shell particles. These patents solve the same problem with similar compositions. One skilled in the coated particles for pharmaceutical use would look to similar references to describe what coating thickness are routinely used and/or inherently provided by standing coating techniques of the art.

In response to appellant's argument that the references fail to show certain features of appellant's invention, it is noted that the features upon which appellant relies (i.e., the increase selectivity of the coating to potassium over competing ions, or a coating that is designed to increase the amount of potassium) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Appellant repeatedly argues that the '665 patent does not solve the problem of the instant claims namely appellant endeavor to develop an oral potassium binder with increased selectivity. However the claims do not recite this limitation and as previously argued the specification does not support such a limitation. The claims are drawn to a composition comprising coated microparticles

having a core and coating. The core is a cation exchange resin and the coating is a crosslinked polymer giving the coating a specific thickness. The ‘494 patent provides an oral composition comprising a coated ion exchange resin, where the coating is open to various well known polymers, and thickness of the coating can and should be controlled during processing. The patent discloses that the coating should not disintegrate and be more permeable to monovalent cations than to higher valances. The '665 patent provides a microparticle formulation comprising a crosslinked coating where the coating thickness is controlled through processing, and provides a stable protection for the core product. The formulation is used to remove compounds from the body (col. 9, lin. 40-45, col. 10, lin. 10-17). The ‘494 patent discloses that surfactants can be used as coating materials, and the '665 patent provides specific surfactants that are biocompatible polymers. These polymers are used to control entry of specific compounds into and out of the cell core (col. 8, lin. 20-58). The coatings of the ‘665 patent are used in a similar way to that of the ‘494 patent, namely permeability selection.

In response to appellant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the appellant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

As can be seen the '494 patent provides a similar pharmaceutical composition as the instant claims where the core and coating is specifically designed to provide selective

permeability. The ‘665 patent provides a specific coating material (suggested by the ‘494 patent) that provides the same function as required by the ‘494 patent. The thickness can be controlled as seen in the ‘665 patent and is uniform despite the size of the core, meaning that permeability and transmission can remain constant and more controlled. For these reasons it would have been obvious to combine the prior art as described above. It would have been obvious to coat the cation-exchange core of the '494 patent with the uniform and crosslinked coating of the '665 patent since both patents remove compounds from the body by allowing the desired compound to permeate the coating and bind to the core. These patents solve the same problem in the same way, specifically binding compounds that permeate through a membrane and removing said compounds from the body by using coated core-shell formulations. For these reasons the claims remain obviated.

**The combination of the '494, '665 and '590 does not obviate the instant claims since the '590 patent does not address the problem of the instant invention.**

Regarding this argument, it remains the position of the Examiner that the combination of the ‘494, 665 and 590 patents continue to obviate the instant claims. As discussed above the ’494 and ‘665 combination discloses a pharmaceutical formulation comprising a core and coating where the coating is of a specific thickness in relation to the core and provides selective permeability to the core. Appellant argues that since the ‘590 patent does not address these issues, it does not obviate the instant claims. However the ‘590 patent is not applied to address these issues as they have been fully addressed and met by the combination of the ‘494 and ‘665 patents. The ‘590 patent is applied to show the level of skill in the art regarding the treatment of

hyperkalemia. The ‘590 patent discloses a method of treating hyperkalemia using a liquid formulation comprising cation exchange resin emulsions. Addressing the limitations of claim 40, it would have been obvious to use the combination of the ’494 and ‘665 patent to treat hyperkalemia since the combination would be a cation exchange rein and emulsions are suggested. For these reasons the claims remain obviated.

**The combination of the '494, '665, ‘960 and '339 patents cannot obviate the instant claims since they do not address the same problem as the instant claims or invention.**

Regarding this argument, it remains the position of the Examiner that the proposed combination would obviate the instant claims. As discussed above the ‘494/ ‘665 combination discloses a microparticulate formulation comprising coated ion exchange resin where the coatings regulate the permeability of ions to the core. This can be achieved by the material or the thickness. The thickness is controlled and manipulated to achieve optimum permeability via the thickness as disclosed in the '665 patent. The combination discloses a wide variety of polymers useful for coatings including polyethylene polymers and crosslinked block copolymers. The combination is silent to vinyl or acrylic polymers, however these polymers are common in the art as seen in the '960 and '339 patents. The ‘960 patent discloses coated ion exchange resin where the exchange resin comprises polystyrene copolymers and the coating is a crosslinked acrylic polymer. The coated resins are used to treat hypocholesteremia. The ‘339 patent discloses a core-shell polymer material that can comprise a variety of polymers that would coat the core including crosslinked polyvinylpyrrolidone. Appellant continue tot argue that these polymers would not address the inventions problem of allowing increased permeability of

potassium to would. Again application is reminded that such a limitation is not present in the claims and is not supported by the specification. Assuming *en arguendo* that the claims required such a limitation, the '494 patent clearly discloses that the coating must allow for the permeability of lower valent ionic over higher valent ions.' The '665 patent further controls the permeability of the coating membrane by controlling the thickness of the coating and making it uniform for every particle. As such the problem of controlling the permeability of the outer coating by controlling the thickness of the outer coating and by providing such a coating thickness and ratio to the core has been solved and addressed by the initial prior art combination of the '494 and '665 patents. The supporting patents merely show the level of skill in the art of microparticles, regarding the inclusion of acrylic and vinyl polymers. These polymers would be incorporated into the combination of '494 and '665 combination. Their thickness would be controlled through the process of the '665 patent and allow for a controlled permeability into the core as described in the '494 and '665 patents. This combination would have been obvious since each patent discloses similar coating materials such as polyethylene block copolymers and acrylic acid copolymers. For these reasons the claims remain obviated.

**(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Michael G. Hartley/

Supervisory Patent Examiner, Art Unit 1618

Conferees:

/MICAH-PAUL YOUNG/
Examiner, Art Unit 1618

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615